NOTE THAT IF THIS AMENDMENT IS DEEMED NON-RESPONSIVE DUE TO A FAILURE TO ADDRESS POINT 4B, APPLICANTS WILL PETITION THE MATTER TO THE GROUP DIRECTOR.

The examiner has then rejected claims 1, 3, 4, 8, 10, 11, 14, 15, 16, 18, 19 and 50 under 35 USC §112, first paragraph, as allegedly being non-enabled.

Claim 7 was not included in this rejection, so it is presumed that claim 7 is enabled. Hence, if any lack of enablement rejection against 7 is presented in any subsequent action, should that action be deemed final, applicants will petition for its withdrawal.

The examiner correctly describes the claims at page 3, paragraph 3. The examiner then goes on to concede that applicants teach 4 nucleic acid molecules which meet the criteria set forth in the claims, but argues that because of the hybridization terminology in the claims, "an indeterminate number and combination of nucleic acid substitutions in SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 24 and SEQ ID NO: 25 by an indefinite number of nucleic acid molecules capable of hybridizing even under stringent conditions to a nucleic acid of cDNA and genomic sequence of TIF" are covered.

Applicants are not in a position to state whether or not an "indefinite number" of nucleic acid molecules are encompassed by the claims, and point out that the examiner has not provided any support for this contention.

Further, there are no rules as to how many examples must be provided to support a broad claim. As is pointed out, supra, applicants provide four examples of suitable nucleic acid molecules.

The specification also teaches what molecule should be considered within the scope of the claim, i.e., the nucleic acid molecules:

(i) must induce T cells;

(ii) must activate STAT3; and,

(iii) must hybridize to at least one of four molecules under defined conditions.

The specification provides detailed examples for determining if a given nucleic acid molecule satisfies each of the given requirements. One of ordinary skill in the art could, without undue experimentation, determine which nucleic acid molecules satisfy all three of these criteria.

The examiner has cited to Doerks in support of her position. Doerks deals with the problem of predicting protein function based upon computer records. The paper describes the

pitfall of doing computer searching due to misleading annotations in the computer data bases searched.

Applicants do not see how this is relevant to the claims. Applicants have set forth, clearly and unequivocally, how one of ordinary skill in the art could test a given nucleic acid molecule to determine if it satisfies the recited criteria. Presumably, it is possible that a given nucleic acid molecule will satisfy two, but not all three of the criteria listed supra. Since applicants describe how to determine this routinely, the fact that some molecules may be found that satisfy some, but not all of the criteria irrelevant. Experimentation is permitted, and a claim is still enabled.

The examiner relies on applicants own specification, allegedly as showing unpredictability. The examiner cites to murine TIF beta

> "induction by IL-9 of murine TIF beta which has high homology to murine TIF alpha (and therefore hybridizes to murine TIF alpha under stringent conditions) is much lower than expression of TIF alpha."

With respect to this statement and to the extent it is understood, the following can be said. First, there is no requirement in the claim that the nucleic acid molecule be induced by IL-9. Second, assuming that the claim did require it, the claim does not require a specific level of expression. The examiner admits that the expression of the murine TIF beta did occur, albeit at a low level. Does this mean the molecule does not induce T cells? Does it mean it does not activate STAT3? The examiner provides no proof of this. The examiner does admit that the hybridization requirement is satisfied. The examiner has simply not made out a prima facie case. Relying on murine TIF-beta is not sufficient, because the data available on the molecule suggest that it does fall within the claim. Even if it did not, this means that of the 5 molecules disclosed in the specification, 80% of them satisfy the claim. There is no requirement of 100% satisfaction.

With respect to the argument presented on page 4, it appears that the examiner has simply ignored the experiments described in the specification. Claims are not considered in a vacuum; rather, the specification must be considered as a whole. When one does so, the specification clearly enables the claims.

The examiner goes on at great length with a theory that "the structural basis for activation of STAT3" must be provided to satisfy enablement. There is no such requirement in the statute. Further, the hybridization language clearly provides structural information.

The rejection at page 4 segues into a written description rejection. This rejection, however, is clearly improper, as being completely contrary to USPTO policy.

Attached hereto is a copy of Example 9 of the guidelines. This example is precisely on point with the subject claims. Should the examiner disagree, then the examiner is called upon to explain why Example 9 does NOT apply. A sequence is disclosed. Hybridization conditions are disclosed, defined, and recited in the claims. The encoded protein, is disclosed. As such, the bases for the rejections are completely improper, and the rejection should be withdrawn.

With respect to the next rejection, which is a new matter rejection, the examiner is invited to review page 28, line 16, through page 29, line 18 of the specification, especially, page 29, lines 5-18. In fact, to facilitate the examiner's review, the entire text is provided here:

> "A preferred aspect of the invention are isolate nucleic acid molecules whose complement hybridize to SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, or SEQ ID NO: 24 under stringent conditions. "Stringent conditions," as used herein, refer, for example, to hybridization at 65°C in buffer (3.5xSSC), 0.02% Ficoll, 0.02% polyvinylpyrrolidone, 0.02% bovine serum albumin, 25mM NaH_2PO_4 (pH7), 0.1% SDS, 2mM EDTA, followed by a final wash at 2xSSC, room temperature and then 0.1xSSC/0.2xSDS at temperatures as high as, e.g., about 65°C. more stringent conditions, such as 0.1xSSC, can also be used. These nucleic acid molecules encode proteins of about 17-22 kD as determined by SDS-PAGE, which activates STAT proteins, such as STAT1, STAT3 and/or STAT5. In glycosylated form, these proteins can range from about 17 to about 30 kilodaltons, as determined by SDS-PAGE."

The examiner is called upon to explain why this does not support the claims, and how a new matter rejection can be supported.

At point 8, the examiner rejects claims 1, 3, 4, 7, 8, 10, 11, 14-16, 18, 19 and 50. This is the first rejection of claim 7. The examiner states that incorporating the language of page 29 into the claims would obviate the rejection. Claim 1 has been so amended.

Claim 1 has also been amended to provide antecedent support for claim 7.

A terminal disclaimer regarding U.S. Patent No. 6,331,613 is provided; thereby obviating the double patenting rejection.

Given the action, claim 7 is clearly now allowable. If this is not the case, a detailed explanation why it is not is required. All other rejections have been addressed and overcome as well.

Allowance of this application is believed proper and is urged.

Respectfully submitted,

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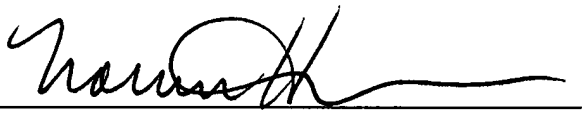

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probes may or may not be labeled, as a matter of choice for the user. Hence, one can determine, for example, if, following administration of IL-9, the cytokine is still efficacious, by determining if the nucleic acid molecule of the invention is present. This type of assay can be adapted, for quantitative studies, wherein one determines, for example, either if a cell is sensitive to IL-9, and if so, how sensitive it is. One can also use the proteins of the invention to phosphorylate STAT proteins such as STAT1 , STAT3 and/or STAT 5. This in turn results in dimerization of the STAT protein, followed by migration to the nucleus to provoke the effect that these STAT proteins have on cells.

One could also use these molecules to test the efficacy of IL-9 agonists or antagonists when administered to a subject, such as a subject suffering from lymphoma , an immune system disorder such as an allergy, acquired immune deficiency syndrome, autoimmune diabetes, thyroiditis, or any of the other conditions described in , e.g, US Patent No. 5,830,454; 5,824,551, and pending application Serial No. 08/925,348, filed on September 8, 1997 now allowed, all of which are incorporated by reference. The molecules can also be used to mediate the role of IL-9 in these and other conditions. To elaborate, since IL-9 induces TIFs, the TIFs are useful as IL-9 activity mediators. Thus, a further aspect of the invention is a method to determine activity of endogenous IL-9, such as in situations where excess IL-9 activity is implicated, such as asthmas, allergies, and lymphomas. One can also block or inhibit IL-9 activity by blocking or inhibiting TIF or TIF activity, using, e.g., antisense molecules, antibodies which bind to TIF, or other antagonists of these molecules. For example, m uteins of TIF, which bind to the TIF receptor but do not activate it, therby inhibiting IL-9 induced activity, are a feature of the invention. Examples of

e.g. expression vectors, the necessary common attribute is the ORF (SEQ ID NO: 2).

Weighing all factors including (1) that the full length ORF (SEQ ID NO: 2) is disclosed and (2) that any substantial variability within the genus arises due to addition of elements that are not part of the inventor's particular contribution, taken in view of the level of knowledge and skill in the art, one skilled in the art would recognize from the disclosure that the applicant was in possession of the genus of DNAs that comprise SEQ ID NO: 2.

Conclusion: The written description requirement is satisfied.

Example 9: Hybridization

Specification: The specification discloses a single cDNA (SEQ ID NO:1) which encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity. The specification includes an example wherein the complement of SEQ ID NO: 1 was used under highly stringent hybridization conditions (6XSSC and 65 degrees Celsius) for the isolation of nucleic acids that encode proteins that bind to dopamine receptor and stimulate adenylate cyclase activity. The hybridizing nucleic acids were not sequenced. They were expressed and several were shown to encode proteins that bind to a dopamine receptor and stimulate adenylate cyclase activity. These sequences may or may not be the same as SEQ ID NO: 1.

Claim:

An isolated nucleic acid that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO: 1,

wherein said nucleic acid encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity.

Analysis:

A review of the full content of the specification indicates that the essential feature of the claimed invention is the isolated nucleic acid that hybridizes to SEQ ID NO: 1 under highly stringent conditions and encodes a protein with a specific function. The art indicates that hybridization techniques using a known DNA as a probe under highly stringent conditions were conventional in the art at the time of filing.

The claim is drawn to a genus of nucleic acids all of which must hybridize with SEQ ID NO: 1 and must encode a protein with a specific activity.

The search of the prior art indicates that SEQ ID NO: 1 is novel and unobvious.

There is a single species disclosed (a molecule consisting of SEQ ID NO: 1) that is within the scope of the claimed genus.

There is actual reduction to practice of the disclosed species.

Now turning to the genus analysis, a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs. Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of

skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention.

Conclusion: The claimed invention is adequately described.